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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,860	01/07/2002	Jose R. F. Corvalan	ABGENIX.051A	5403

37915 7590 05/19/2004

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,860	CORVALAN ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 22-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 22-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, and 22-45 are pending.

2. Applicant's election with traverse of Group 35, Claims 1-2 and 21 (now claims 1-2, and 22-45) drawn to a human monoclonal antibody that binds to platelet derived growth factor D comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49, filed 3/8/04, is acknowledged. The traversal is on the grounds that (1) all of the groups are related as all of the claims relate to human monoclonal antibodies or antigen-binding portions thereof that specifically bind to Platelet Derived Growth Factor D (PDGFD) share a common human VH-18 family gene and a common JH6B family gene. (2) Applicants have discovered that human monoclonal antibodies or antigen-binding portions thereof that specifically bind to PDGFD and are encoded by a human VH1-8 family gene and a JH6B family gene show the strong ability to neutralize the growth promoting effects of PDGFD. The claimed antibodies not only share a common structure but that structure has been demonstrated to correlate with improved neutralizing function. This is not found persuasive because of the reasons set forth in the restriction mailed 11/4/03. The various human monoclonal antibodies that bind to Platelet Derived Growth Factor D comprise different heavy chains and light chains encoded by different VH family gene, JH6B family gene and D5-18 family gene. Each antibody entails separate searches in the amino acid and nucleic acid databases. What was once a relative simple search has now become far more burdensome, due both to performing the computer search and the analysis of the search results. The sequence search and literature search, both particularly relevant in this art, is not coextensive. A search of one monoclonal antibody comprising a distinct heavy chain of SEQ ID NO: 48 and light chain of SEQ ID NO: 49 would not necessarily identify prior art relevant to the examination of other monoclonal antibodies comprising different heavy and light chains. It is doubted that applicants would readily accept rejection of other human monoclonal antibodies in view of prior art which reads upon SEQ ID NO: 48 and SEQ ID NO: 49. It is a burden to search more than one invention. Therefore, the requirement of Group 35 (now claims 1-2, and 22-45) and Groups 1-34 is still deemed proper. However, it is noted that applicants have canceled non-elected groups.

3. Claims 1-2, and 22-45, drawn to a human monoclonal antibody that binds to platelet derived growth factor D comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49 are being acted upon in this Office Action.

4. Claims 24-29 and 34-39 are objected to under 37 CFR 1.821(d) because SEQ ID NO is required.

5. The disclosure is objected to for failing to comply with the requirement of 37 C.F.R. 1.821(d), SEQ ID NO is required for Figures 23-40, Appropriate correction is required.

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 22, 24-32, 34-43, and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a human monoclonal antibody or antigen binding portion thereof that binds to Platelet Derived Growth Factor D (PDGFD) comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49; The said human monoclonal antibody or antigen binding portion thereof wherein the heavy chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the amino acid sequence of GYTFTSYDIN, CDR2 consists the amino acid sequence of INPNSGNTDYAQKFQ, and CDR3 consists the amino acid sequence of GFGYSYNYDYYYGMDV; The said human monoclonal antibody or antigen binding portion thereof wherein the light chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the amino acid sequence of RASQSVSSSYLA, CDR2 consists the amino acid sequence of ATSSRAT, and CDR3 consists the amino acid sequence of QQYGSSPCS, and a labeled human monoclonal antibody or antigen binding portion thereof mentioned above wherein said monoclonal antibody or antigen binding portion thereof is labeled with a detectable marker for detection assay, **does not** reasonably provide enablement for any human monoclonal antibody

that binds to any Platelet Derived Growth Factor such as any number and/or combination of heavy chain and light chain, any number and/or combination of CDR1, CDR2 and CDR3 from heavy or light chain, any human monoclonal antibody that binds to any Platelet Derived Growth Factor "further comprises any sequence encoded by any "human D5-18 family gene", any human monoclonal antibody that binds to any Platelet Derived Growth Factor derived from any "human VH1-8 gene", and any "JH6B family gene" as set forth in claims 1-2, 22, 24-32, 34-30, 32-40 or with a detectable label (claims 31, 41 and 45) and composition comprising said monoclonal antibody or antigen-binding fragment thereof (claims 42, 43, and 45) for any purpose. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a human monoclonal antibody or antigen binding portion thereof that binds to human Platelet Derived Growth Factor D (PDGFD) comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49. The said human monoclonal antibody or antigen binding portion thereof of the heavy chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the amino acid sequence of GYTFTSYDIN, CDR2 consists the amino acid sequence of INPNSGNTDYAQKFQ, and CDR3 consists the amino acid sequence of GFGYSYNYDYYYGMDV. The said human monoclonal antibody or antigen binding portion thereof of the light chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the amino acid sequence of RASQSVSSSYLA, CDR2 consists the amino acid sequence of ATSSRAT, and CDR3 consists the amino acid sequence of QQYGSSPCS. The specification further discloses a labeled human monoclonal antibody or antigen binding portion thereof that binds to Platelet Derived Growth Factor D (PDGFD) comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID

NO: 49 wherein said monoclonal antibody or antigen binding portion thereof is labeled with a detectable marker. The specification further discloses various hybridoma cell lines producing monoclonal antibodies comprising the specific heavy chain and the specific light chain amino acid sequences such as the ones shown in Figures 3-21.

The specification does not teach how to make any human monoclonal antibody mentioned above that bind to all PDGF-D. The specification merely discloses human PDGF-D as an immunogen for making the human monoclonal antibody. There is insufficient guidance about the structure of other PDGF-D, much less about the binding specificity of the claimed antibody.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed immunogen would generate human monoclonal antibody that binds to all PDGF-D.

Further, the claims encompass any number and/or combination of heavy and light chain (claims 1-2), any number and/or combination of CDR1, CDR2, and CDR3 from immunoglobulin heavy chain (claims 24-26 and 34-36), any number and/or combination of CDR1, CDR2, and CDR3 from immunoglobulin light chain (claims 27-29, and 37-39). There is insufficient guidance as to which combination of heavy and light chain or which combination of CDR1, CDR2, CDR3 from which heavy chain and/or combination of CDR1, CDR2, CDR3 from which light chain that the undisclosed antibody would maintain the same binding specificity as the claimed antibody that binds specifically to human PDGF-D.

Janeway et al teach that the association of different heavy and light chain variable regions from the binding site (See page 3:21, last paragraph, in particular). However, the function of an antibody molecule is dependent on its three dimensional structure, which in turn is dependent on its primary amino acid sequence. Changing the amino acid sequence of an antibody may adversely affect its activity. Likewise, fragments of the antibody may not retain the appropriate

three dimensional structure necessary to foster binding activity. Moreover, a change in the DNA sequence coding for the antibody may affect the ability of the cell containing the DNA sequence to express, secrete or assemble the antibody. The exact residues comprising CDRs are difficult to define and do not necessarily correspond to all the residues in the hypervariable regions, as defined by the Kabat numbering system. There are also critical framework residues which are important in positioning the CDRs for interaction with antigen or which are involved in interactions between the heavy and light chains. Therefore, it is not clear that any combination of CDR regions from heavy and light chains will have the asserted utility of binding to human PDGF-D, without further guidance from the specification. Further, there is insufficient working example demonstrating any combination of CDR regions will have the asserted binding specificity to all PDGF-D, in turn, would be useful for any purpose.

Further, the term "comprising" is open-ended. It expands the CDR1, CDR2 and CDR3 regions of heavy and light chain (claims 24-29 and 34-39) to include additional amino acid residues at either end. Given the indefinite number of undisclosed amino acids to be added, there is insufficient guidance as to which amino acids to be added and whether the resulting antibody maintains the same binding specificity.

With regard to claims 22, 30, 32 and 42, the specification provides insufficient guidance as to which particular VH1-8 family gene and JH6B family gene encode the claimed antibody without the nucleotide sequence. Further, the term "gene" as defined by Merriam-Webster's Online Dictionary, 10th Edition is a segment of DNA that is involved in producing a polypeptide chain; it can include regions preceding and following the coding DNA as well as introns between the exons. The specification provides insufficient guidance as to the introns as well as exons encoding the undisclosed human monoclonal antibody. In addition to the lack of guidance for the genes mentioned above, there is a lack of guidance as to which undisclosed "sequence encoded by which gene of the human D5-18 family gene without the nucleotide sequence (claim 22). Given the indefinite number of human monoclonal antibody, the is insufficient in vivo working example demonstrating that all disclosed antibody is effective for treating all disease. Since the binding specificity of all human monoclonal antibody mentioned above is not enabled, it follows that any composition comprising said antibody is not enabled. It also follows that all undisclosed monoclonal antibody comprises a detectable marker are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 1-2, 22, 24-32, 34-43, and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of any human monoclonal antibody that binds to any Platelet Derived Growth Factor such as any number and/or combination of heavy chain and light chain, any number and/or combination of CDR1, CDR2 and CDR3 from heavy or light chain, any human monoclonal antibody that binds to any Platelet Derived Growth Factor "further comprises any sequence encoded by any "human D5-18 family gene", any human monoclonal antibody that binds to any Platelet Derived Growth Factor derived from any "human VH1-8 gene", and any "JH6B family gene" as set forth in claims 1-2, 22, 24-32, 34-30, 32-40 or with a detectable label (claims 31, 41 and 45) and composition comprising said monoclonal antibody or antigen-binding fragment thereof (claims 42, 43, and 45).

The specification discloses only a human monoclonal antibody or antigen binding portion thereof that binds to human Platelet Derived Growth Factor D (PDGFD) comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49. The said human monoclonal antibody or antigen binding portion thereof of the heavy chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the amino acid sequence of GYTFTSYDIN, CDR2 consists the amino acid sequence of INPNSGNTDYAQKFQ, and CDR3 consists the amino acid sequence of GFGYSYNYDYYYGMDV. The said human monoclonal antibody or antigen binding portion thereof of the light chain comprises CDR1, CDR2 and CDR3 wherein the CDR1 consists the

amino acid sequence of RASQSVSSSYLA, CDR2 consists the amino acid sequence of ATSSRAT, and CDR3 consists the amino acid sequence of QQYGSSPCS. The specification further discloses a labeled human monoclonal antibody or antigen binding portion thereof that binds to Platelet Derived Growth Factor D (PDGFD) comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49 wherein said monoclonal antibody or antigen binding portion thereof is labeled with a detectable marker. The specification further discloses various hybridoma cell lines producing monoclonal antibodies comprising the specific heavy chain and the specific light chain amino acid sequences such as the ones shown in Figures 3-21.

With the exception of the specific human monoclonal antibody that binds to human PDGF-D comprising the specific combination of heavy and light chains, the specific combination of CDR1-3 regions in the heavy and light chains, there is insufficient written description about the structure associated with function such as the binding specificity of all human monoclonal antibody mentioned above that bind to all PDGF-D. The specification merely discloses human PDGF-D for making the human monoclonal antibody. There is inadequate written description about the structure of other PDGF-D, much less about the binding specificity of the claimed antibody.

Further, the claims encompass any number and/or combination of heavy and light chain (claims 1-2), any number and/or combination of CDR1, CDR2, and CDR3 from immunoglobulin heavy chain (claims 24-26 and 34-36), any number and/or combination of CDR1, CDR2, and CDR3 from immunoglobulin light chain (claims 27-29, and 37-39). There is inadequate written description about which combination of heavy and light chain (claims 1-2) that forms the undisclosed antibody and whether the antibody has the same binding specificity as the human monoclonal antibody that binds to human PDGF-D comprising comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49. Likewise, there is inadequate written description about which combination of CDR1, CDR2, CDR3 forms the heavy chain (claims 24-26 and 34-36) and which combination of CDR1, CDR2, CDR3 forms the light chain (claims 27-29, and 37-39) of which undisclosed antibody and whether the antibody would have the same binding specificity as the human monoclonal antibody that binds to PDGF-D comprising comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49. Further, the term "comprising" is open-ended. It expands the CDR1, CDR2 and CDR3

regions of heavy and light chain (claims 24-29 and 34-39) to include additional amino acid residues at either end. The specification provides insufficient written description about the undisclosed amino acids to be added, and whether the resulting antibody maintains the same binding specificity as the human monoclonal antibody that binds to PDGF-D comprising comprises a heavy chain amino acid sequence comprising SEQ ID NO: 48 and a light chain amino acid sequence comprising SEQ ID NO: 49.

With regard to claims 22, 30, 32 and 42, the specification provides insufficient written description about which particular VH1-8 family gene and JH6B family gene encode the claimed antibody or which undisclosed human monoclonal antibody that binds to PGDF-D is derived from which particular human V_H1-8 family gene and J_H6B family gene without the nucleotide sequence (claims 22, 32 and 42). Further, the term "gene" as defined by Merriam-Webster's Online Dictionary, 10th Edition is a segment of DNA that is involved in producing a polypeptide chain; it can include regions preceding and following the coding DNA as well as introns between the exons. However, the specification provides insufficient written description about the introns as well as exons encoding the undisclosed human monoclonal antibody, let alone a gene from the human VH1-8 and JH6B gene that encode any human monoclonal antibody or antigen binding portion thereof that specifically binds to all Platelet Derived Factor D (PDGF-D). In addition to the lack of a written description about the genes mentioned above, there is insufficient written description about the "sequence encoded by which gene of the human D5-18 family gene without the nucleotide sequence (claim 30). Since the binding specificity and structure of all human monoclonal antibody mentioned above are not adequately described, it follows that any composition comprising said antibody is not adequately described. It also follows that all undisclosed monoclonal antibody comprises a detectable marker are not adequately described.

Finally, the specification discloses only human PDGF-D as an immunogen for making the claimed antibody that binds to human PDGF-D, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 23-29, 31-39 41, 44, and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "having" as recited in claims 23-29, 31-39 and 44 is indefinite and ambiguous. The office interprets the term "having" as open-ended and, if intended to be open-ended, prefers the term "comprising". if intended to be close-ended, prefers the term "consisting of".

The "detectable marker" in claims 31 has no antecedent basis in base claim 22 because the antibody in claim 22 is not a labeled antibody. It is suggested that claim 31 be recited "A labeled human monoclonal antibody wherein the antibody or antigen binding portion thereof of claim 22 is labeled with a detectable marker", for example.

The "detectable marker" in claims 41 has no antecedent basis in base claim 32 because the antibody in claim 32 is not a labeled antibody.

The "detectable marker" in claims 45 has no antecedent basis in base claim 42 because the antibody in claim 42 is not a labeled antibody

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 22, 30-32, 40-43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 6,706,687 (March 16, 2004; PTO 892) in view of Green et al (Nature Genetics 7: 13-21, May 4, 1994; PTO 892).

The '687 patent teaches monoclonal antibody and antigen binding portion thereof that binds to platelet derived growth factor D (PDGFD) (See column 10, lines 63-44, in particular). The reference further teaches the reference antibody is labeled with a detectable marker such as FITC for detection assay (See column 11, lines 10-23, in particular). The reference antibody is useful as inhibitor or agonist of PDGF-D or diagnostic assays (See column 10, line 61-63, in particular).

The claimed invention in claims 22, 32 and 42 differs from the reference only that the monoclonal antibody that specifically binds to Platelet Derived Growth Factor is human monoclonal antibody instead of mouse monoclonal antibody and is encoded by or derived from a human VH1-8 family agene and a JH6B family gene.

The claimed invention in claims 30, 40 and 43 differs from the reference only that the human monoclonal antibody that specifically binds to Platelet Derived Growth Factor further comprises a sequence derived from human D5-18 family gene.

Green et al teach a method of making human antibody that binds to any antigen of interest wherein the reference antibody is encoded by or derived from a one of the human VH1-8 family agene such as VH6 and a JH6B family of gene such as J6 family gene (See Table 2, page 16, clone μ100, in particular). The reference antibody further comprises a sequence encoded by a human D family of gene such as TGGTTATTAC (See Table 2, page 16, clone μ100, in particular). The reference teaches that fully human monoclonal antibody is that the antibody is less immunogenic, and thus more suited for repeated administration (See page 20, column 1, last paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make human monoclonal antibody as taught by Green et al that binds to PGDF-D as taught by the '687 patent for a fully human monoclonal antibody encoded by human VDJ genes. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Green et al teach that fully human monoclonal antibody is that the antibody is less immunogenic, and

thus more suited for repeated administration (See page 20, column 1, last paragraph, in particular). The '687 patent teaches antibody PDGF-D is useful as inhibitor or agonist of PDGF-D or diagnostic assays (See column 10, line 61-63, in particular).

15. Claims 1, 2, 23-29, 33-39 and 44 are free of prior art.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

18. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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